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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,320	HADDEN, JOHN W.	
	Examiner	Art Unit	
	Sharon Wen	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *17-23 and 30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

DETAILED ACTION

1. Claims 1-32 are pending.

Election/Restrictions

2. Applicant's election of Group I and, CY and INDO, the specific administering step of **unilaterally** administering, the specific administering step of **before surgery or radiotherapy**, the specific tumor antigen of **exogenous**, and the specific cancer of **head and neck squamous cell carcinoma** (H&NSCC) in the Response to Election / Restriction filed on 11/26/2007 and the species of **IL-1, IL-2, IL-6, IL-8, IL-12, IFN-δ, TNF-α, GM-CSF, and G-CSF** as the combination of natural cytokine mixture (NCM) during a phone conversation with Applicant's representative, Kenneth Kohn, on 01/30/2008, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon further consideration, the search has been extended to include the specific administering step of **bilateral** administration and **during recurrence**.

It is noted that Groups III-IV (claims 18-20) set for in the Restriction Requirement, mailed 09/04/2007, read on a method for treating cancer. However, as stated previously in the Restriction Requirement, given the difference in the preambles between the elected Group I (claims 1-16 and 24-29) and non-elected Groups III-IV (claims 18-20) and the absence of essential ingredients in Groups III-IV (claims 18-20); and in view of Applicant's non-response to Examiner's request to distinguish between Groups III-IV, claims 18-20 are therefore withdrawn.

Applicant is again invited to distinguish between the elected Group I (claims 1-16 and 24-29) and non-elected Groups III-IV (claims 18-20). If the method steps and endpoints are the same or nearly the same as they read on immunotherapy of cancer, then claims 18-20 will be rejoined.

3. Claims 17-23 and 30-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-16 and 24-29 are currently under examination as they read on a method of immunotherapy to treat H&NSCC by administering natural cytokine mixture (NCM), cyclophosphamide (CY) and indomethacin (INDO).

Priority

4. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, USSN 10/015,123, fails to provide adequate written support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In view of the **Request for Certificate of Correction**, filed 01/16/2006, and **Certificate of Correction - Post Issue Communication**, issued 03/27/2006, for the priority Application, USSN 10/015,123, it is noted that interferon-delta (IFN-δ) was changed to interferon-gamma (IFN-γ) in both the specification and patented claims due to inadvertent typographical errors as asserted by Applicant. Therefore, priority application USSN 10/015,123, does not support the recitation of "interferon-delta (IFN-δ)" in claims 1-11, 14-16 and 24-29 of the present application.

It is noted that the present application appears to claim subject matter disclosed in prior Application USSN 10/637,869 filed 08/08/2003. However, a reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if Applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c).

See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., **continuation**, **divisional**, or **continuation-in-part**) of all nonprovisional applications.

5. Given the issues discussed in the above section of ***Priority***, the priority date for claims 1-11, 14-16 and 24-29 is deemed the effective filing date of priority application USSN 10/637,869, i.e., 08/08/2003.

The priority date for claims 12 and 13 is deemed the effective filing date of provisional application, USSN 60/243,912, i.e., 10/27/2000.

Should Applicant disagree with the Examiner's factual determination above, it is incumbent upon Applicant to provide a showing that specifically supports the instant claim limitations.

Applicant is invited to amend the first line of the specification to up-date the priority of this application.

Subject to New Matter

6. In the interest of compact prosecution, the following is noted with respect to Applicant's previous efforts to correct the disclosure and recitation of "interferon-delta (IFN-δ)" with "interferon-gamma (IFN-γ)".

Consistent with the comments in the Section on ***Priority*** above, the only disclosure of "interferon-gamma (IFN-γ)" in the instant disclosure is on pages 25-26 of the instant specification in Table I as follows.

> "Cytokines were assayed using commercial ELISA kits (Quantikine.TM., R & D Systems, Inc., Minneapolis, Minn.)(See, Table I). Biological activity of the NCM of the present invention was confirmed using a murine cytotoxic T-cell line (CTLL-2), which was originally developed as an indicator of biological activity of IL-2.

Table I: NCM cytokine contents for five lots used at INCAN

Lot No. Designations:	IL-2 Activity IU/mL	IL-1β pg/Ml	Il-2 pg/mL	IFN-γ pg/mL
1	188	439	7228	1802
2	189	444	7253	1854
3	197	427	7575	NT
4	168	370	6449	1929
5	171	449	6576	2527
Mean	183	426	7016	2028
S.D.	12	32	482	337

"

Other than this one instance of assaying for "interferon-gamma (IFN-γ) in the natural cytokine mixture (NCM) of the present invention, there is no reference to "interferon-gamma (IFN-γ)" in the context of anti-cancer treatment methods in the instant disclosure as filed.

Assaying for "interferon-gamma (IFN-γ) in a natural cytokine mixture (NCM)" is not the same as using "interferon-gamma (IFN-γ) in a natural cytokine mixture (NCM) in anti-cancer treatment methods, as currently claimed in the instant application.

The only interferon described for use in the claimed anti-cancer methods in the instant specification as filed is interferon-delta (IFN-δ).

Applicant is notified that attempts to correct the instant disclosure of "interferon-delta (IFN-δ)" with "interferon-gamma (IFN-γ)" would be subject to a rejection under 35 USC 112, first paragraph, written description / new matter.

The specification as filed does not provide a sufficient written description of the use of interferon-gamma (IFN-γ)" in a natural cytokine mixture (NCM) in anti-cancer treatment methods, as currently claimed in the instant application. The specification does not provide blaze marks nor direction for the instant methods encompassing the use of "interferon-gamma (IFN-γ)" in the instant anti-cancer treatment methods. Amending the instant disclosure or claims with "interferon-gamma (IFN-γ)", which is not clearly disclosed in the specification as-filed, would change the scope of the instant disclosure as-filed. Such limitations which did not appear in the specification, as filed, would introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is reminded that amending the instant disclosure must meet two criteria, that is, both the error must be obvious and the correction must be obvious as well.

Here in the instant application, attempts to amend/correct the disclosure and recitation of "interferon-delta (IFN-δ)" with "interferon-gamma (IFN-γ)" would not be obvious, given that there is insufficient support in the instant application for the use of "interferon-gamma (IFN-γ)" in anti-cancer treatment methods and that there is insufficient support for correcting interferon-delta (IFN-δ)" with "interferon-gamma (IFN-γ)" (e.g., over other interferons such as interferon-alpha or interferon-beta as well as over other cytokines).

Sequence Compliance

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825 (see specification on page 8, lines 12-13, e.g., "EADPTGHSY" and "EVDPIGHLY"). However, this application fails to comply with the requirements set forth on the attached **Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures**.

Applicant is required to fulfill these requirements.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821-1.825 in response to this Office Action.

Specification

8. Applicant is requested to review the application for the use of trademarks, embedded hyperlinks and/or other form of browser-executable code.

Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference.

Claim Rejections - 35 USC § 112 second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2-9, 13 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 2-9 recite the limitation "said administering step" in claim 1. There is **insufficient antecedent basis** for this limitation in the base claim.

B) Claims 13 and 16 are indefinite in the recitation of "**A synergistic anti-cancer treatment / method**" because this "synergistic" limitation is relative in nature, which renders the claims indefinite in that the "synergistic" limitation is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree or endpoints to reasonably apprise one of ordinary skill in the art of the metes and bounds of the invention.

For example, the specification does not set forth nor define the metes and bounds nor the nature of dosages of the ingredients nor the treatment effects encompassed by this claimed recitation.

Also, it is noted that the specification discloses the following.

Summary of the Invention

"The present invention further provides a **synergistic** anti-cancer treatment by administering an effective amount of CY and INDO in combination with an NCM described herein." (See page 4-5 of specification.)

Detailed Description of the Invention

"In another embodiment of the present invention, there is provided a method of immunotherapy to treat cancer by administering an effective amount of CY and an effective amount of INDO. Another embodiment of the present invention provides a **synergistic** anti-cancer treatment method by administering an effective amount of a CY and an effective amount of a NSAID, wherein the NSAID can be, but is not limited to, INDO, Ibuprofen, celecoxib (Celebrexe®), rofecoxib (Vioxx®), CoxII inhibitors, combinations thereof, and the like." (See page 16 of specification)

"A **synergistic** anti-cancer treatment is also provided by the present invention, wherein the treatment includes the steps of administering an effective amount of CY and INDO in combination with a NCM. The NCM can include, but is not limited to, IL-1, IL-2, IL-6, IL-8, IL-12, IFN-.delta., TNF-.alpha., GM-CSF, G-CSF, recombinants thereof, combinations thereof, and any other similar cytokine known to those of skill in the art." (See page 17 of specification)

Role of the NSAID in Conjunction with CY in Example 7

"In four patients a dose of the NCM was given that was considered inactive (See, FIG. 10, 15 units column) in conjunction with INDO and CY. No survivals were observed, yet two patients had minor response (<50%, but >25% tumor shrinkage) and all four showed moderate pathological changes in the tumor specimen with tumor reduction and fragmentation as well as lymphoid infiltration (See, Table IV). INDO can increase lymphoid infiltration and tumor reduction in some patients (See, Panje, 1981, and Hirsch, et al., 1983), but it has not been accepted clinically as a useful therapy in H&N SCC. Similarly, CY at this dose is not considered clinically active in H&N SCC. The activity of INDO and CY alone can be considered surprising in the magnitude and type of tumor response. INDO and CY are considered as a **synergistic** combination for employment with other forms of immunotherapy." (See page 36 of specification.)

From a reading of the instant specification, it appears that the "synergistic anti-cancer treatment" is simply adding "an effective of cyclophosphamide and an effective amount of indomethacin / NSAID" in combination with a natural cytokine mixture and/or with other forms of immunotherapy.

Applicant is invited to clarify whether the "synergistic anti-cancer treatment" is simply adding "an effective amount of cyclophosphamide and an effective amount of indomethacin / NSAID" in combination with a natural cytokine mixture (NCM) and/or with other forms of immunotherapy or whether the claimed "synergistic anti-cancer treatment" reads on particular dosages of the ingredients and/or treatment effects.

If the recitation of the claimed synergistic anti-cancer treatment is not limited to characterizing the adding "an effective of cyclophosphamide and an effective amount of indomethacin / NSAID" in combination with a natural cytokine mixture and/or with other forms of immunotherapy, then the claims do not recite and the specification does not set forth guidelines as to defining and determining the metes and bounds of "synergistic anti-cancer treatment / method" as it reads on dosages of the ingredients and /or treatment endpoints encompassed by the claimed methods.

For examination purposes and consideration under prior art, "a synergistic anti-cancer treatment / method" reads on simply adding an effective of cyclophosphamide (CY) and an effective amount of indomethacin (INDO) / NSAID in combination with a natural cytokine mixture and/or with other forms of immunotherapy.

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add New Matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

11 The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 24-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Given that Applicant elected the species of **exogenous tumor antigens** to which the claimed method of eliciting an immune response, the following grounds of rejection is set forth here.

The present claims are directed to a method of eliciting an immune response to exogenous tumor antigens by administering NCM with or without CY and/or INDO. However, the specification as-filed does not provide sufficient enabling description for eliciting an immune response without administering any antigen.

A person of ordinary skill was well-aware at the time of the invention was made that antigen is needed to elicit an immune response to the antigen. For example, Janeway et al. teach that the fundamental induction of an immune response, known as immunization, is routinely performed in experiments by injecting the test antigen into animal or human subjects (*see ImmunoBiology: the Immune System in Health and Disease*, 3rd edition, 1997, Current Biology Ltd., London, UK and Garland Publishing Inc., New York, NY, USA. Page 2:2).

The instant specification discloses that that NCM is used as an adjuvant in addition to exogenous tumor antigens to immunize cancer patient against tumor antigens (see page 18, lines 28-30 and page 20, lines 29-31). In addition, the specification discloses examples of eliciting delayed type hypersensitivity in mice and human by administering specific cancer antigens in conjunction with NCM, CY and INDO as adjuvant (see pages 43-44, Example 12). The specification does not provide sufficient *in vivo* or *in vitro* evidence showing administering NCM, CY and/or INDO without any exogenous tumor antigen would elicit an immune response to any exogenous tumor antigen.

The instant application provides insufficient guidance and instruction on the necessary steps one of skill would need to administer the adjuvant (i.e., NCM, CY and/or INDO) without any exogenous tumor antigen and achieve the intended results, i.e. elicit an immune response against exogenous tumor antigens. In view of the unpredictability of the art and insufficient working examples provided by Applicant, it would require undue amount of experimentation for a skilled artisan to practice the claimed invention.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Given the recitation of "endogenous" in the claim, it is noted that cancer patients who receive immunotherapy would developed immune response to endogenous tumor antigens.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-13 and 24-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Meneses et al. (*Arch. Pathol. Lab. Med.* 1998, 122:447-454, see entire document).

While Applicant's species election of **IL-1, IL-2, IL-6, IL-8, IL-12, IFN-δ, TNF-α, GM-CSF, and G-CSF** as the specific combination of natural cytokine mixture (NCM) is acknowledged, given the Markush language in the present claims and the applicability of this reference in the rejection under 35 USC 103, the following grounds of rejection is set forth herein.

Meneses et al. teach a method of treating head and neck squamous cell carcinoma (H&NSCC) comprising administering a NCM comprising IL-1, IL-2, IL-6, IL-8, IL-10, IL-12, TNF-α, colony stimulating factor (CSF), interferon gamma (IFN-γ) and effective amounts of CY and INDO, in which 150 units of IL-2 equivalence by ELISA is administered, specifically (see, e.g., page 447, Abstract "**Patients**" and page 448, Material and Methods, "**Natural Cytokine Mixture**" and "**IRX-2 Treatment Schedule**"). In addition, the administration is prior to surgery and during recurrence and both unilaterally and bilaterally for cases of midline lesions (see pages 448-449 "**IRX-2 Treatment Schedule**").

The prior art also teaches recombinant IL-2 used in treatment (see page 447, last paragraph). It is noted that the recitation of "recombinant" in the present claim is a product-by-process limitation which reads on the cytokine that is made by a recombinant process. Since the reference teaches the cytokines of the present invention, the same cytokines made by a recombinant process would also be anticipated by the reference.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

It is also noted that although the prior art does not explicitly teach "a synergistic anti-cancer treatment" or "a method of eliciting an immune response to tumor antigens", *per se*, given the same or nearly the same method step of administering a NCM plus CY and INDO for treating H&NSCC, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See *Bristol-Myers Squibb Company v. Ben Venue Laboratories* 58 USPQ2d 1508 (CAFC 2001).

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 1-11 and 14-16, 24-29 are rejected under 35 U.S.C. 103(a) as being obvious over Meneses et al. (*Arch. Pathol. Lab. Med.* 1998, 122:447-454) in view of Rees et al. (US 20030007955 A1).

It is noted that the dependent claims of claim 1 are included herein as they read on the elected species of the NCM cytokine combination, i.e. IL-1, IL-2, IL-6, IL-8, IL-12, IFN-δ, TNF-α, GM-CSF, and G-CSF.

The teaching by Meneses et al. has been discussed supra.

Meneses et al. differs from the present claims in that it does not teach IFN-delta (IFN-δ), granulocyte-macrophage colony stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) in the natural cytokine mixture. However, it is obvious to a person or ordinary skill in the art at the time of the invention was made to include IFN-δ, GM-CSF and G-CSF in immunotherapy for treating cancer because these are well-known therapeutic proteins for treating cancer as exemplified by Rees et al. (see entire document, in particular, see paragraphs [0003]-[0005], [0017]-[0020], [0105]-[0106] and [0295]).

In particular, Rees et al. teach a method of treating squamous cell carcinoma comprising administering a mixture of therapeutic proteins selected from a list of cytokines what include IL-1, IL-2, IL-6, IL-8, IL-12, **IFN-δ**, TNF-α, **GM-CSF**, and **G-CSF** (see paragraphs [0017] and [0020]).

Given that both Meneses and Rees teach treating head and neck cancer (see discussion of Meneses et al. above and paragraph [0027] of Rees et al.,) using a cytokine mixture, it would have been obvious to one of skill in the art to include IFN-δ as taught by Rees et al. in the cytokine mixture as taught by Meneses et al. for the same purpose of treating head and neck cancer because there is a finite number of IFN types to choose from, i.e., (IFN-α, IFN-β, IFN-γ, IFN-δ).

Similarly, given that Meneses et al. teach CSF in the cytokine mixture, it would have been obvious to substitute GM-CSF and G-CSF as taught by Rees et al. in the cytokine mixture for the same purpose of treating head and neck cancer because GM-CSF and G-CSF are commonly known examples of CSF.

Lastly, Rees et al. teach that such modification would have been apparent to those skilled in the art (see paragraph [0295]).

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-2, 10-16, 24-29 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-9 of U.S. Patent No. 6,977,072 ('072). Although the conflicting claims are not identical, they are not patentably distinct from each for the following reasons:

Both sets of claims are drawn to a method comprising administering NCM plus CY and INDO. Patent '072 is directed to treating cancerous lesions which is anticipated by the elected species of H&NSCC of the present application. Although the recitation of "unblocking immunization" in claim 1 of '072 is not in the claims of the present application, given the same or nearly the same method steps recited in more sets of claims, they would have anticipated or rendered obvious of one and another.

In addition, the patented claims anticipate the instant claims in view of the Markush language recited in the instant claims.

Conclusion

19. No claim is allowed.

20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Wen whose telephone number is (571) 270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571)272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner

February 7, 2008

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Application No. 10/567,320

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 CFR 1.821 - 1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).

☒ 7. Other: see Office Action section "Sequence Compliance"

Applicant must provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d)

For questions regarding compliance with these requirements, please contact:

For Rules Interpretation, call (703) 308-1123
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Please return a copy of this notice with your response.